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SPECIAL REPORTS

Appropriate Electrophysiologic Study and Treatment of Patients With the Wolff-Parkinson-White Syndrome*

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Since Wolff et al. (1) first described the electrocardiogram (ECG) recognized 2 years later by Holzmann and Scherf (2) to be associated with ventricular pre-excitation by way of conduction over an accessory atrioventricular (AV) connection, an enormous amount of information has accumulated about what we now call the Wolff-Parkinson-White or ventricular pre-excitation syndrome. The recent advances in the diagnosis and treatment of this syndrome have particularly added to the wealth of information concerning its clinical management. Therefore, the North American Society of Pacing and Electrophysiology (NASPE) thought it timely to develop a consensus concerning the evaluation and treatment of patients with this syndrome.

A NASPE policy conference on these aspects of the Wolff-Parkinson-White Syndrome was held on May 14, 1986 in New Orleans, Louisiana. After a presentation by Dr. Pedro Brugada (Maastricht, The Netherlands) entitled "Who Should be Studied?", by Dr. John J. Gallagher (Charlotte, North Carolina) entitled "Of What Should the Electrophysiologic Study Consist?" and by Dr. George J. Klein (London, Ontario, Canada) entitled "What is Appropriate Therapy?", a thorough discussion was held and a consensus reached. The following represents the formal report of this meeting and constitutes NASPE's current recommendations concerning these three questions. The recommendations are provided in an effort not only to establish standards for care of patients with this syndrome, but also to educate the practicing medical community about what constitutes a contemporary approach to the diagnosis and treatment of abnormalities of rhythm and conduction associated with this syndrome. It is appreciated that these recommendations will have to be reevaluated at a pace commensurate with that of new advances in our understanding of this syndrome.

I. Who Should Undergo Electrophysiologic Testing?

A. *Introduction*

The question of which patients with the Wolff-Parkinson-White syndrome should be studied electrophysiologically is generally determined by each patient's clinical presentation and the contemplated therapeutic approach. Although there is a clear consensus for most presentations, some gray areas remain. The overriding concern at all times should be to identify those patients who are potentially or overtly at risk for sudden death because of the presence of one or more accessory atrioventricular (AV) connections with properties that will permit very rapid ventricular response rates in the presence of atrial fibrillation or atrial flutter. This is so very important because of the well recognized propensity for these supraventricular arrhythmias to develop at some time in many patients with this syndrome.

B. *Noninvasive Electrophysiologic Assessment*

Because clues to the anterograde effective refractory period of the accessory AV connection or connections may be present from assessment of simple, noninvasive techniques, careful use of these techniques may provide sufficient data so that invasive electrophysiologic study may not be necessary. The surface ECG may show varying manifestations of the Wolff-Parkinson-White syndrome. Ventricular pre-excitation may be overt, and the typical pattern may be

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persistent or intermittent. It is important to recognize that ventricular pre-excitation patterns may mask or mimic patterns of myocardial infarction, conduction block or ventricular hypertrophy. Inapparent (or latent) pre-excitation is diagnosed when ventricular pre-excitation is not evident in control 12 lead ECG tracings, but becomes manifest with various maneuvers or during electrophysiologic studies. In patients with one or more concealed accessory AV connections, the baseline ECGs show no evidence of ventricular pre-excitation, but the possibility of only retrograde conduction over these connections can be proved during invasive electrophysiologic studies. In patients with inapparent ventricular pre-excitation, various maneuvers that slow or block accessory AV nodal conduction (that is, vagal maneuvers or administration of calcium channel blockers) may allow expression of ventricular pre-excitation. Prolonged ambulatory ECG (Holter) monitoring may be of benefit for the diagnosis of those with intermittent ventricular pre-excitation.

Noninvasive electrophysiologic testing may be of value in assessing the functional characteristics of the accessory AV connection or connections. For example, the sudden normalization of the QRS complex in the ECG during sinus rhythm is usually associated with a prolonged anterograde effective refractory period of the accessory AV connection. Disappearance of ventricular pre-excitation with administration of class IA antiarrhythmic drugs usually reflects the presence of an accessory AV connection with a prolonged effective refractory period. These agents may therefore be of help in distinguishing ventricular pre-excitation patterns from confounding patterns of myocardial infarction, bundle branch block or ventricular hypertrophy. When abrupt or intermittent (2:1, 3:1) cessation of accessory AV connection conduction occurs during exercise testing, it usually indicates the presence of a long effective refractory period of the accessory AV connection bypass pathway.

It should be emphasized that patients who, by this sort of noninvasive electrophysiologic assessment, appear to have a long anterograde effective refractory period of the accessory AV connection still may suffer from rapid, hemodynamically unstable arrhythmias. Furthermore, none of the noninvasive tests are infallible in predicting the electrophysiologic properties of an accessory AV connection. Therefore, further studies may be indicated either for diagnostic purposes in patients with suspected ventricular pre-excitation or in patients with clear ventricular pre-excitation, but in whom the characteristics of the electrophysiologic substrate are uncertain.

C. *Invasive Electrophysiologic Assessment*

Programmed electrical stimulation of the heart combined with recordings of electrical activation (electrograms) using standard cardiac electrophysiologic techniques can quickly and accurately provide information about the presence, number, location and functional characteristics of accessory AV connections and their likely relation to a patient's symptoms. During programmed stimulation of the heart, the shortest ventricular cycle length (RR interval) associated with 1:1 anterograde conduction by way of one or more accessory AV connections and the anterograde effective refractory period of such connections can be measured. Also, atrial fibrillation can be artificially induced before and after autonomic manipulation. The observation of a long anterograde effective refractory period of an accessory AV connection (>270 ms) makes it unlikely that fast ventricular rates during atrial fibrillation will occur as a result of conduction over that connection. Therefore, it is very unlikely that this arrhythmia will cause severe symptoms or degenerate into ventricular fibrillation because of the presence of one or more accessory AV connections. Conversely, a very short anterograde effective refractory period of one or more accessory AV connections or short RR intervals that result from conduction over such connections during induced atrial fibrillation (<250 ms), are accompanied by an increased risk of severe symptoms or degeneration of the arrhythmia into ventricular fibrillation. The positive predictive value for sudden death of either of these findings is unknown, but likely to be low. However, patients who do not exhibit either of these findings may nevertheless suffer from other rapid, hemodynamically unstable arrhythmias, most commonly accessory AV reentrant (reciprocating) tachycardia.

Electrophysiologic studies are also useful to understand the effects of antiarrhythmic drugs and to select drug therapy in patients with ventricular pre-excitation. However, electrophysiologic studies are mandatory in patients being considered for surgical or electrical ablation of one or more accessory AV connections or the His bundle, or for use of an antitachycardia pacemaker. Patients being considered for surgical correction of either congenital or acquired cardiac disease in the presence of known ventricular pre-excitation also should undergo electrophysiologic testing to determine the number, location and characteristics of accessory AV connections. This is important not only because of the possibility of surgically interrupting the accessory accessory AV connections at the time of surgery, but also because of the high incidence of postoperative arrhythmias such as atrial fibrillation and atrial flutter, which, depending on the characteristics of the accessory AV connections, may result in life-threatening arrhythmias in the postoperative period.

Some additional uses of invasive electrophysiologic study involving special circumstances are controversial but merit consideration. These include possible assessment of risk in athletes or those engaged in sporting activities, in airline pilots or those who operate mass transportation vehicles and in the elucidation of unusual forms of cardiac hypertrophy and incomplete bundle branch block.

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II. Of What Should the Electrophysiologic Study Consist?

A. Introduction

The appropriate electrophysiologic study of a patient with known or suspected Wolff-Parkinson-White syndrome should be tailored to the clinical situation. Thus, a study aimed simply at diagnosis might be limited to establishing the presence of an accessory AV connection and the demonstration of induction of an accessory AV reentrant tachycardia and atrial fibrillation using a single electrode catheter in the heart or the esophagus. In contrast, a study intended as a guide to ablative therapy must establish the number, type, location and participation of accessory AV connections in question. The following sections present current recommendations for procedures to be performed for the most complete electrophysiologic study. The extent of an appropriate study should be considered on a patient by patient basis.

B. Description of a Complete Electrophysiologic Study

1. General remarks. Complete electrophysiologic study utilizes multiple electrode catheter and ECG recordings in concert with programmed stimulation of the atria and the ventricles. The initial study is best performed in the drug-free state. The essentials of the study can be stated as a series of questions that a complete study must address: 1) Is pre-excitation present? 2) What are the number, type and locations of accessory AV connections? 3) What are the arrhythmias observed (spontaneous or induced)? 4) Does an accessory AV connection participate in the observed arrhythmia or arrhythmias? 5) What are the functional properties of the normal and accessory accessory AV connections? 6) What are the effects of drugs, autonomic manipulations, exercise and pacing? 7) Are there associated anomalies (anatomic or electrophysiologic)?

2. ECG recordings. A minimum of three ECG leads, I, aVF (or II or III) and V_1, should be recorded throughout the study, and a standard 12 lead ECG should be recorded during atrial pacing from multiple sites in both atria and during induced or spontaneous atrial fibrillation or atrial flutter. This will enhance recognition of different QRS complex configurations in the ECG associated with ventricular pre-excitation, and allow the onset of ventricular activation to be identified accurately. In addition, a 12 lead ECG should be recorded during induced and spontaneous AV reentrant tachycardia and during any other tachycardia that might occur.

3. Placement of electrode catheters. With use of standard techniques, multipolar electrode catheters should be placed to record or pace, or both, from the coronary sinus, right ventricle, high right atrium and His bundle. Occasionally, a quadripolar catheter for recording and pacing from the left ventricle is also required.

4. Identification and localization of accessory AV connections. Techniques that identify or confirm the presence of one or more accessory AV connections should be used. If such connections are present, their location should be established, and their characteristics, including participation in spontaneous and induced arrhythmias, should be determined. *To this end:*

a) The earliest site of retrograde atrial activation during accessory AV reentrant tachycardia or ventricular pacing, or both, should be identified.

b) Recording of electrograms from multiple sites in the coronary sinus allows the retrograde ventriculoatrial (VA) activation sequence at the level of the left AV groove (within the limits of its relation to the coronary sinus) to be obtained. When access to the coronary sinus is not possible, electrograms from the left atrium can be obtained from an electrode catheter passed across the interatrial septum, from the right or left pulmonary artery or from the esophagus, but these recording sites do not accurately reflect events at the level of the left AV groove.

c) With use of an electrode catheter, electrograms should be recorded from multiple sites along the circumference of the tricuspid anulus.

d) Whenever an apparent earliest atrial activation site is identified during retrograde VA conduction, every effort should be made to bracket activation at that site, that is, to demonstrate that nearby sites on either side of the apparent earliest atrial activation site are activated later than the site in question.

e) The configuration of the delta wave during maximal ventricular pre-excitation can be helpful as a rough guide to accessory accessory AV connection location. It is of limited value for distinguishing septal from paraseptal accessory AV connections and in the presence of coexisting cardiac abnormalities such as ventricular hypertrophy, congenital defects and multiple accessory AV connections. The value of delta wave analysis becomes more forceful when combined with atrial pacing from selected sites, because pacing in the vicinity of an accessory AV connection results in the shortest stimulus to delta wave interval in the ECG and the greatest degree of ventricular pre-excitation. More important, the potential for unmasking multiple accessory AV connections is enhanced.

5. Recording other variables. Recording of a time mark at short intervals, preferably every 10 ms, is strongly recommended to permit accurate measurement of electrophysiologic intervals. The ability to monitor systemic blood pressure should be available and used at the discretion of the study physician.

6. A recommended study sequence. Although the exact sequence of the study must be tailored to the patient, two principles are constant: early in the study, the presumptive

location of the accessory AV connection or connections should be demonstrated because this will determine the optimal site for assessing refractoriness of such connections; maneuvers likely to precipitate atrial fibrillation (which might necessitate cardioversion) generally should be performed late in the study. There are several appropriate sequences one can follow to perform a complete electrophysiologic study. *The following is one such sequence.*

a) A typical study may begin with ventricular pacing at a cycle length that clinically will permit a prolonged period of pacing (for example, 500 or 400 ms), with determination of the sequence of retrograde atrial activation, principally at the level of the AV groove. Electrograms then should be monitored from the right atrium, His bundle and coronary sinus (preferably at least two electrograms). Right ventricular pacing at increasing rates to the point of retrograde block or hemodynamic compromise should then be carried out, carefully noting any tendency for eccentric retrograde atrial activation to appear. Pharmacologic block of the AV node with verapamil or esmolol may be required at some time during the study to bring out eccentric VA conduction. The appearance of an eccentric sequence of atrial activation during ventricular pacing immediately suggests the presence of an accessory AV connection.

b) Next, induction of AV reentrant tachycardia should be attempted. If the arrhythmia is successfully induced, the sequence of atrial activation should be determined again. When the observed sequence of retrograde atrial activation is initiated in the septal region, differentiation of retrograde by way of an accessory AV connection from retrograde conduction through the node may be difficult and requires introduction of ventricular premature beats during the tachycardia when the His bundle is refractory to make a clear distinction. Repeated inductions of tachycardia are recommended in an effort to elicit bundle branch block aberration during the tachycardia to obtain diagnostic information concerning the presence and location of the accessory AV connection or connections. Prolongation of the VA interval during an accessory AV reentrant tachycardia by the appearance of a bundle branch block pattern in the ECG suggests participation of the ventricle in the reentrant circuit, but it is observed only when delay or block is present in the conduction system responsible for activating the ventricular insertion of the accessory AV connection, and may not be seen with septal accessory AV connections.

Ipsilateral bundle branch block results in prolongation of the VA interval by >35 ms in the case of free wall accessory AV connections (right or left). In the case of septal accessory AV connections, VA interval prolongation of ≤25 ms occurs with left bundle branch block (posteroseptal) or right bundle branch block (anteroseptal).

c) One may then proceed to determination of the effective refractory periods of the atria, ventricles, normal AV conduction system and accessory AV connection or connections. The refractory period of an accessory should be assessed by stimulating as closely as possible to that accessory connection. Because of cycle length dependence, refractory period determination should be carried out by introducing premature beats after a train of 8 to 12 basic drive beats at a minimum of two pacing cycle lengths, for example, 500 and 400 ms.

d) If induction of a sustained AV reentrant tachycardia has not been achieved at this point, a closer look at the apparent "weak link" of the tachycardia circuit is appropriate. A very long retrograde effective refractory period in the accessory AV connection or long anterograde effective refractory period in the AV node may suggest that an orthodromic AV reentrant tachycardia is unlikely to be induced in the baseline state. In this case, an infusion of isoproterenol might allow "enhancement" of conduction of the appropriate structure by decreasing its effective refractory period.

Assuming that a sustained AV reentrant tachycardia is induced, the effects of premature ventricular and atrial beats introduced during diastole may be useful in understanding, localizing and characterizing the tachycardia circuit. If sustained AV reentrant tachycardia had been induced without the need for isoproterenol administration, determination of refractory periods may be usefully repeated after administering isoproterenol as a continuous drip infusion, usually 1 to 3 μg/min, so as to decrease sinus cycle length by 20 to 25%, thereby permitting an estimation of potential conduction over any accessory AV connections during atrial fibrillation in the presence of increased circulating catecholamines.

e) To elicit maximal electrocardiographic ventricular pre-excitation in the ECG, pacing during sinus rhythm from multiple atrial sites in the right atrium, atrial septum and coronary sinus should be performed, preferably during the recording of a 12 lead ECG. These recordings facilitate both prediction of the site of anterograde insertion of an accessory AV connection and recognition of multiple accessory AV connections. Assuming that all sites are paced at an identical cycle length shorter than sinus cycle length, the shortest stimulus to delta wave interval in the ECG and the greatest degree of ventricular pre-excitation in the ECG leads should be produced by pacing in the immediate vicinity of the accessory AV connection if it is capable of conducting at the selected pacing cycle length.

f) Having accomplished the aforementioned objectives, the study should then move on to maneuvers likely to precipitate atrial fibrillation. Rapid atrial pacing to the point of either 2:1 AV block or induction of atrial fibrillation should then be performed and the ventricular response determined. It is desirable to include elective induction of atrial fibrillation during the baseline study because the shortest interval between the onset of two consecutive pre-excited ventricular (that is, QRS) complexes (the so-

called shortest pre-excited RR interval) has been identified as an independent predictor of risk for sudden death. Shortest pre-excited RR intervals <250 ms were uniformly demonstrated in patients resuscitated from ventricular fibrillation associated with the Wolff-Parkinson-White syndrome. This observation depends on induction of atrial fibrillation lasting at least several minutes. If the shortest pre-excited RR intervals are >250 ms, a pharmacologic stress should be considered in the form of isoproterenol as a continuous intravenous drip infusion, usually 1 to 3 μg/min, to decrease the sinus length by 20 to 25%, and then reprecipitate atrial fibrillation.

g) Once all the baseline observations have been collected, selected parts of the study may be repeated to assess a variety of autonomic manipulations, antiarrhythmic drug effects or the suitability of an antitachycardia device.

III. Therapy

A. Therapeutic Options for Patients With the Wolff-Parkinson-White Syndrome

1. The therapeutic options for the Wolff-Parkinson-White syndrome include: (a) no therapy; (b) pharmacologic therapy, either intermittent (given only during symptoms) or long-term (given prophylactically); (c) surgical interruption of the accessory AV connection or connections; (d) implantation of an antitachycardia device, generally a cardiac pacing device, to terminate the tachycardia; (e) His bundle ablation; and (f) accessory AV connection ablation with a transvenous catheter technique.

2. The therapeutic decision depends to a great extent on the clinical presentation and expertise with the various therapeutic options present at the treatment facility. For example, surgical ablation of an accessory AV connection is only recommended when the volume and experience of the local group result in a success rate approximating 90 to 95% and a mortality rate <2% in the patient without concomitant severe heart disease. In addition, catheter ablation techniques directed at affecting accessory AV connections are considered investigational at this time, but appear promising, at least for posteroseptal accessory AV connections.

B. Recommended Therapy

In this discussion, patients are categorized by clinical presentation. Each therapeutic modality is classified as generally preferable, acceptable or generally inappropriate. The recommendations are made with the assumption that a thorough knowledge of the mechanism of the arrhythmias and the functional properties of the normal and accessory accessory AV conduction systems are known.

1. Presentation with atrial fibrillation and a rapid ventricular response rate (that is, the shortest RR interval due to AV conduction through an accessory AV connection or connections is ≤250 ms), with or without development of ventricular fibrillation. Because this arrhythmia is generally accepted as potentially life threatening, surgical ablation of the accessory AV connections is generally preferred when feasible and no other mitigating circumstances are present. Medical therapy demonstrated to be beneficial by electrophysiologic testing is an acceptable alternative. Current antitachycardia devices do not address the problem of atrial fibrillation and, therefore, are considered inappropriate as primary therapy. Neither His bundle ablation nor no therapy is appropriate.

2. Presentation with AV reentrant tachycardia utilizing an accessory AV connection, known short (≤270 ms) anterograde effective refractory period of the accessory AV connection and known short (≤250 ms) shortest RR interval due to AV conduction through an accessory AV connection. In these patients, although the presenting clinical problem is AV reentrant tachycardia, the short pre-excited RR interval indicates that a potentially life-threatening ventricular arrhythmia might occur should spontaneous atrial fibrillation or atrial flutter develop. In fact, in the presence of one or more accessory AV connections, AV reentrant tachycardia frequently evolves to atrial fibrillation. Therefore, therapy that addresses this possibility should be considered. Surgical ablation or, depending on the location of the accessory AV connections, catheter ablation of the connections is acceptable and may be a preferred option. Similarly, medical therapy demonstrated to be beneficial by electrophysiologic testing is acceptable. Currently available antitachycardia devices are generally inappropriate as primary therapy because of their known risk of precipitating atrial fibrillation when used to terminate AV reentrant tachycardia. Similarly, either His bundle ablation or no therapy is generally inappropriate, as neither addresses the issue of atrial fibrillation with the potential for a rapid ventricular response rate due to anterograde conduction through one or more accessory AV connections.

3. Presentation with AV reentrant tachycardia utilizing an accessory AV connection with or without atrial fibrillation and an associated "slow" ventricular response rate, and with a known long anterograde effective refractory period of the accessory AV connection and a known long shortest RR interval resulting from AV conduction through an accessory AV connection. This arrhythmia is not considered to be life threatening. Therefore, all therapeutic options directed at treating the AV reentrant tachycardia except those that might decrease the anterograde effective refractory period of the accessory AV connection or connections, such as can occur with use of a digitalis preparation, are considered acceptable. Surgical interruption of the accessory AV connections in the patient with AV reentrant tachycardia and atrial fibrillation generally prevents both arrhythmias in the absence of underlying organic heart disease. However, in considering surgical therapy, it is important to demonstrate the presence of an AV reentrant tachycardia because sur-

gery probably will not address the problem of atrial fibrillation if the atrial fibrillation exists as a primary arrhythmia.

Electrophysiologic testing is useful in guiding therapy, although empirical therapy is acceptable in this group if severe symptoms or complications have not accompanied episodes of tachycardia. Use of an antitachycardia device is acceptable provided atrial fibrillation is not a clinical problem. His bundle ablation is acceptable for therapy of AV reentrant tachycardia, although other treatments that do not result in pacemaker dependence should be strongly considered first. Of course, no pacemaker may be required because satisfactory and stable AV conduction may occur through the accessory AV connection. No therapy may be appropriate in patients with infrequent and mildly symptomatic episodes.

4. Presentation without tachycardia (that is, asymptomatic) and with a known long anterograde effective refractory period of the accessory AV connection or long shortest RR interval due to AV conduction through an accessory AV connection. It is generally agreed that the patient with this condition is not at risk for sudden cardiac death due to a rapid ventricular response rate as a result of conduction to the ventricles through one or more accessory AV connections during atrial fibrillation. Therefore, no treatment is the preferred therapeutic option. In general, any treatment for this category of patient directed at affecting the accessory AV connection is inappropriate. However, because certain occupations may not allow the existence of ventricular pre-excitation electrocardiographically, surgical correction is sometimes considered for this reason.

5. Presentation without tachycardia (that is, asymptomatic) but with a short anterograde effective refractory period of the accessory AV connection or short anterograde RR interval as a result of AV conduction through an accessory AV connection, or both. There are insufficient data to provide firm guidelines to manage patients in this category. Although such patients are known to have a sporadic risk of sudden death, the general prognosis is still good, and the finding of a short effective refractory period of the accessory AV connection has a low predictive value. In this context, no treatment must at least be considered acceptable. Treatment with surgery or medication may be acceptable under some circumstances, although insufficient data are available for firm recommendations. Currently available antitachycardia devices are generally inappropriate. It is recognized that difficult clinical decisions must be made, especially in the so-called high risk patient such as an airline pilot or professional athlete. The finding of a long anterograde effective refractory period of the accessory AV connection or connections in such patients is helpful, but the finding of a short one is more difficult to deal with. Prophylactic therapy, either medical or surgical, is considered acceptable in these patients, although we note again that at this time, insufficient data are available to permit firm recommendations.

6. Absence of symptoms in patients undergoing heart surgery. It is generally agreed that electrophysiologic assessment is indicated for such patients, especially because arrhythmias such as atrial fibrillation and atrial flutter commonly complicate the immediate postoperative period. Concomitant surgical interruption of the accessory AV connection or connections should be considered, particularly in patients with a short effective refractory period of an accessory AV connection or a short RR interval associated with AV conduction through an accessory AV connection, but also in patients with an inducible AV reentrant tachycardia that is shown to utilize the accessory accessory AV connection.

7. Presentation with incessant AV reentrant tachycardia. All effective therapies are considered acceptable, including surgical correction of the accessory connection, medical therapy and His bundle ablation. Currently available antitachycardia devices usually do not provide effective therapy of incessant AV reentrant tachycardia. Giving no therapy is acceptable in the short term for asymptomatic patients with normal left ventricular function. However, such patients require close follow-up, which includes monitoring of left ventricular function in a manner analogous to that used in volume overload syndromes. Furthermore, it can be anticipated that, for most such patients, persistent tachycardia will ultimately result in ventricular dilation accompanied by deterioration of left ventricular function. Therefore, no therapy of this rhythm is rarely appropriate.

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